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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,889	06/04/2007	Peter Svete	33668US-PCT	3731

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EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
4131	

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03/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,889	SVETE ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 4th 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,18 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/28/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

3DETAILED ACTION

Status of Claim:

Claims 1-10, 18 and 19 are pending and is subject of this office action.

Receipt is acknowledged of a preliminary amendment filed on 08/28/2006 in which claims 5-10 were amended, claims 11-17 were cancelled and new claims 18-19 were added.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 08/28/06. The Examiner has considered the reference cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449. The "Search report" on 1449 has been lined out because it is not a published document and therefore cannot have a date of publication which is required for a citation in the non-patent document area of 1449.

Specification

The use of the trademark Syloid™ has been noted in the claims and specification of the instant application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claims 1-10, 18-19 of the instant application are drawn towards a pharmaceutical composition comprising an active pharmaceutical ingredient such as potassium salt of losartan which exists in the first polymorph susceptible to degradation or interconversion into one or more other polymorphs forms, and further comprising a stabilizing substance such as colloidal silicon dioxide.

Claim Rejections - 35 USC § 102 (e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated in Antoncic et al. (US 7271269).

Antoncic discloses a potassium salt of losartan characterized by a powder X-ray diffraction pattern with peaks at about 2θ 6.9, 13.8, 20.6, 24.8, 28.7, 29.2° (Form X) (column 14, lines 14-17) and pharmaceutical composition containing polymorphic forms

of losartan specifically the form exhibiting strongest diffractions at around 2θ 6.9, 13.8, 20.6, 24.8, 28.7, 29.2° (Form X) (column 15, lines 41-42 and lines 63-65). This reads on instant claims 1, 2 and 4.

Antoncic discloses an aspect of their invention where in the pharmaceutical active ingredient of the composition is the amorphous form of losartan (column 17, lines 11-16) (reads on instant claim 3) and film coated tablet formulations of potassium salt of losartan with suitable excipients (column 16, lines 12-21) (reads on instant claim 5). The following examples 52a and 52b disclosed by Antoncic describe the coated tablet formulation of polymorphic forms of potassium salt of losartan. Excipients claimed in the instant claim 1, 6-8 are indicated by arrows in the examples.

EXAMPLE 52a

(Film Coated Tablets)
Composition of a tablet

core	
Losartan potassium	100.000 mg
Silicified Microcrystalline Cellulose	199.200 mg
Croscarmellose Sodium	16.000 mg
Silica Colloidals Anhydrica	3.200 mg
Magnesium stearate	1.600 mg
coating	
Hydroxypropylcellulose	4360 mg
Ethylcellulose	6.540 mg
Triethyl citrate	2.000 mg
Titanium dioxide	1.080 mg
Ferric oxide red	0.620 mg
Talc	3.000 mg
Weight	336.600 mg
*Ethanol	120.000 mg
**Talc	0.220 mg

*Ethanol is removed during the process
**Talc is not included into the coating polishing agent

EXAMPLE 52b

(Film Coated Tablets)

Composition of a Tablet

core	
Losartan potassium	25.000 mg
Silicified Microcrystalline Cellulose	199.200 mg
Croscarmellose Sodium	16.000 mg
Silica Colloidalis Anhydrica	9.200 mg
Magnesium stearate	1.400 mg
coating	
Hydroxypropylcellulose	15.900 mg
Stearic acid	2.100 mg
Triethyl citrate	5.800 mg
Titanium dioxide	1.580 mg
Ferric oxide red	0.020 mg
Talc	1.250 mg
Weight	336.000 mg
*Ethanol	140.000 mg
**Talc	6.236 mg

*Ethanol is removed during the process
**Talc is not included into coating, polishing agent

In example 52a above calculation of % weight of ethyl cellulose by total weight of the pharmaceutical compositions yields a value of 0.13% and in example 52b calculation of % weight of the stearic acid by total weight of the pharmaceutical composition yields a value of 0.2%. Both these values are well within the range claimed in instant claim 6. Calculations of % weight of anhydrous silica (Silica colloidalis Anhydrica) in examples 52a and 52b above yields a value of 10% which is within the range claimed in claim 7-8 of the instant application.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Instant claims 1-3 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dolitzky et al (US 2004/0006237) and Campbell et al (US 5608075) and Antoncic et.al (US 7271269).

Dolitzky teaches polymorphic forms of amorphous losartan potassium (page 1, section (0002) and (0003)) specified in instant claims 1-3. Dolitzky also teaches a pharmaceutical composition containing polymorphic forms of amorphous losartan potassium along with one or more suggested excipients which include colloidal silicon dioxide (0080-0081) specified in instant claim 1. Additionally Dolitzky teaches the

method of treating hypertension in a patient suffering from hypertension by administering to a patient a dosage form of losartan potassium (claim 8 and claim 26, 43) specified in instant claims 18-19.

Campbell teaches the mechanism of action of polymorphic forms of Losartan, in that they are known to inhibit the action of the octapeptide hormone angiotensin II and are useful therefore in alleviating angiotensin induced hypertension. He also teaches that administration of losartan with a non-steroidal anti-inflammatory drug (NSAID) can prevent renal failure which sometimes results from administration of a NSAID (column 1, lines 9-42). This reads on instant claims 18-19.

Antoncic teaches pharmaceutical compositions comprising of polymorphic forms potassium salt of losartan with pharmaceutical excipients which includes colloidal anhydrous silica (see above examples 52a and 52b) as described in the U.S 35 102 (e) rejection above.

What Dolizky, Campbell and Antoncic do not teach is the specific use of a stabilizing substance such as anhydrous silicon dioxide in a pharmaceutical composition to stabilize a polymorphic form of potassium salt of losartan from degradation. Applicant identifies colloidal silicon dioxide as having stabilizing property to stabilize polymorphic forms of potassium salt of Losartan. Stabilizing effect is a property of anhydrous colloidal silicon dioxide. A component and its property cannot be separated. Silicon dioxide when present in compositions as taught by Antoncic (see above examples 52a and 52b) will inherently exhibit its stabilizing property.

Claim 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antoncic et.al (US 7271269) in view of Bharatarajan et.al. (US 2006/0177498)

Antoncic teaches pharmaceutical compositions comprising of potassium salt of losartan with pharmaceutical excipients as described in the above rejection.

What Antoncic does not teach is the exact type of finely divided Silicon dioxide as Syloid™ claimed in instant application.

This deficiency is cured by Bharatarajan, who teaches the use Syloid AL-1 claimed in Instant application as one of the suitable excipients with low moisture content that prohibit uptake of moisture and provide the effect of increased stability of formulations with low water contents excipients (0016, 0025-0026). Bharatarajan also provides Example 3 (0036) where Syloid AL-1 is used in a formulation of ramipril. The differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because it would have been *prima facie* obvious to the skilled artisan to try different types of excipients and known moisture absorbing materials to achieve the desired level of stabilization in the composition. Selection of excipients and the amounts to be used can be readily determined by one of ordinary skilled in the arts based upon experience and consideration of standard procedures and reference work in the field. One would be motivated to do so to achieve the most stable and effective pharmaceutical composition.

The experimental data disclosed by the applicant (Specification pages 11-15) to demonstrate the properties of the claimed composition is noted and acknowledged. Data presented demonstrates the intrinsic stabilizing property of anhydrous finely divided silicon dioxide and cannot be used to overcome the instant rejection.

Conclusion

Claims 1-10, 18 and 19 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 8 am to 5 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SAVITHA RAO
Examiner
Art Unit 4131

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614